## REMARKS

Claims 19, 23-36, 38-42, and 54-56 are pending with Claims 19 and 33 being amended herein. No new matter has been added with the amendments. Support for the amendments can be found in the claims and specification as filed, for example at [0208] of the present application as published.

Rejections under 35 U.S.C. § 103

Claims 19, 23-26, 28, 29, 30-36, 38, 39, and 40-42 were rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 6,040,194 to Chick et al. ("Chick et al.") in view of U.S. Patent No. 6,485,703 to Cote et al. ("Cote et al.") and U.S. Patent No. 6,377,721 to Walt et al. ("Walt et al."). The Examiner states, inter alia, "[I]t would have been obvious for one of ordinary skill in the art to include monitoring of intracellular concentrations of one or more metabolites in the method of Chick and correlating them with blood glucose levels because Cote teaches the importance of monitoring both intra- and extra-cellular analytes . . . In addition, Walt teaches that there are fluorescent dyes (such as acetoxymethyl ester form of BCECF) that are cell membrane permeant, thus allowing intracellular concentrations of analytes to be measured when needed."

Although not acquiescing to this rejection, Applicant respectfully submits that this rejection is moot in light of the present amendments herein. For example, independent Claim 19 presently recites the following:

> 19. A method for monitoring the concentration of one or more metabolites or analytes, the method comprising:
>
> applying a skin sensor composition to a surface of the skin for a predetermined period of time, wherein said skin sensor composition comprises a reporter dye and a marker dye, wherein the wavelength and/or intensity of fluorescence emission or absorbance of said reporter dye varies in proportion to a change in concentration of a metabolite or analyte, and the wavelength and/or intensity of fluorescence emission or absorbance of said marker dye does not vary in proportion to a change in concentration of the metabolite or analyte, and further wherein the marker dye comprises a coumarin;
>
> causing penetration of the skin sensor composition to a depth of about 10 μm, wherein said depth corresponds with the bottom of the dead stratum corneum layer, to about 175 μm, wherein said depth corresponds with the top of the dermal layer, into the epidermis;
>
> monitoring a change in the intracellular concentration of the metabolite or analyte by detecting the change in fluorescence emission or absorbance of the reporter dye and detecting the emission or absorbance of the marker dye using an optical reader; and

> correlating the change in the intracellular concentration of the metabolite or analyte with in vivo blood concentration of the metabolite or analyte.

Applicant respectfully submits that none of the cited references teach or suggest a method for monitoring the concentration of one or more metabolites or analytes as presently claimed in independent Claim 19. For example, Chick et al. discloses using fluorescence resonance energy transfer ("FRET") to measure glucose concentration. Chick et al. explains:

> In FRET, a sample or mixture is illuminated at a wavelength which excites the donor but not the acceptor molecule directly . . . If donor and acceptor are not in sufficiently close proximity, FRET does not occur and emissions occur only at the donor wavelength. If donor and acceptor are in sufficiently close proximity, FRET occurs. The results of this interaction are a decrease in donor lifetime, a quenching of donor fluorescence, an enhancement of acceptor fluorescence intensity, and depolarization of fluorescence intensity. (8:52-62).

Cote et al. also describes a FRET mechanism (e.g., 29:33-30:39). Applicant respectfully submits that Chick et al., Cote et al., and Walt et al., either alone or in combination, do not teach or suggest the method for monitoring the concentration of one or more metabolites or analytes as presently claimed in independent Claim 19. Independent Claim 33 is directed to a method for monitoring in vivo blood glucose levels and recites, inter alia, a skin sensor composition that can include "a reporter dye and a marker dye, wherein the wavelength and/or intensity of fluorescence emission or absorbance of said reporter dye varies in proportion to a change in concentration of glucose, and the wavelength and/or intensity of fluorescence emission or absorbance of said marker dye does not vary in proportion to a change in concentration of glucose, and further wherein the marker dye comprises a coumarin . . ." With respect to Claim 33, Applicant respectfully submits that the above rejection is moot for at least the reasons discussed above with respect to Claim 19.

Claim 27 was also rejected under 35 U.S.C. § 103(a) as being unpatentable over Chick et al., Cote et al., and Walt et al., as applied to Claims 19, 23-26, 28, 29, 30-36, 38, 39, and 40-42 above, and further in view of U.S. Patent No. 5,972,199 to Heller et al. ("Heller et al."). Without acquiescing to this rejection, applicant respectfully submits that Chick et al., Cote et al., Wachtler et al., Walt et al., and Heller et al. do not, alone or in combination, teach or suggest every element recited in the claims as presently amended herein. For example, none of these references teach or suggest a skin sensor composition that can include a reporter dye and a marker dye as presently

claimed herein. Furthermore, it would not be obvious to a person of ordinary skill to modify any of these references to arrive at the independent Claims as presently amended herein.

In view of the foregoing, it is respectfully asserted that Claims 19 and 33 are patentable. Furthermore, all claims depending directly or indirectly from Claims 19 and 33 are also patentable for at least the same reasons as discussed above for their respective independent claim, and also because each claim recites a novel and unobvious combination of elements.

*No Disclaimers or Disavowals*

Although the present communication may include alterations to the application or claims, or characterizations of claim scope or referenced art, Applicant is not conceding in this application that previously pending claims are not patentable over the cited references. Rather, any alterations or characterizations are being made to facilitate expeditious prosecution of this application. Applicant reserves the right to pursue at a later date any previously pending or other broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter found to be specifically disclaimed herein or by any prior prosecution. Accordingly, reviewers of this or any parent, child or related prosecution history shall not reasonably infer that Applicant has made any disclaimers or disavowals of any subject matter supported by the present application.

*Co-Pending Applications of Assignee*

Applicant wishes to draw the Examiner's attention to the following co-pending applications of the present application's assignee.

| Docket No. | Serial No. | Title | Filed |
|---|---|---|---|
| MLA.026CPCPCCC | 11/349,731 | NON-INVASIVE MEASUREMENT OF ANALYTES | Feb. 7, 2006 |

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: April 30, 2009

By: /Lindsey N. Singeo/
Lindsey N. Singeo
Registration No. 61,365
Attorney of Record
Customer No. 20,995
(949) 760-0404

AMEND

7009681
042009